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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,582	01/23/2002	Frederick R. Blattner	960296.95726	5379

7590 01/13/2005

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EXAMINER	
VOGEL, NANCY S	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/057,582	BLATTNER ET AL.	
	Examiner	Art Unit	
	Nancy T. Vogel	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *8-30* is/are withdrawn from consideration.

5)☒ Claim(s) *4,6 and 7* is/are allowed.

6)☒ Claim(s) *1-3 and 5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/25/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-30 are pending in the case.

Receipt of the Information Disclosure Statement on 3/25/04 is acknowledged. Copies of certain of the references listed on the Information Disclosure Statement were not received, and therefore have been struck through and not considered.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-7 in the reply filed on 6/30/04 is acknowledged. The traversal is on the ground(s) that the subject matter of Group I and Groups II-VII is inextricably mixed, and therefore the examiner cannot consider the subject matter of one without considering the subject matter of the other. This is not found persuasive because for the reasons made of record in the restriction requirement, the subject matter of the groups as set forth therein are separate and distinct; for instance, the methods of Groups II-VII set forth distinct methods for manipulating the genome of bacteria, including deleting and inserting DNA, and the bacteria set forth in Group I can be made by a variety of methods. Therefore, the search for the Groups as set forth are not the same, and it would be a burden for the examiner to conduct a thorough search of the diverse methods and bacteria encompassed by the Groups.

The requirement is still deemed proper and is therefore made FINAL.

Claims 8-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or

linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 6/30/04.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, and 5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection is based on the Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, first paragraph "Written Description published in the Federal Register (Volume 66, Number 4, Pages 1099-1111). Claims 1-3 are drawn to a bacteria having a genome that is genetically engineered to be at least 5, 8 or 14% smaller than the genome of its native parent strain, and claim 5 is dependent on claim 1 and further recites DNA or genes which are deleted. Claims 1-3 and 5 are genus claims in terms of bacterial strains having deletions of any genes in the genome resulting in a specified size genome. The disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of

skill in the art cannot envision all the bacteria which have the recited reduced size genome as compared to the native parent strain.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, function characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. The disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all the bacteria, and their genomic structure, that have the recited reduced genome size when compared to the native parent strain. While the specification provides information of regions of E. coli that may be deleted, which result in the recited percentage reduction in genome size as compared to the parent strain while still remaining viable, and methods which may be carried out in order to result in E. coli with a reduced genome size, there is no guidance for carrying out a similar method in bacteria other than E. coli. Furthermore, there is no disclosure of the structure of such a genome other than E. coli, nor a structure-function analysis of the complete genus, or representative members of the genus, which comprises any bacteria, sufficient to shoes that applicants were in possession of the invention as claimed. One cannot envision the structure of such genomes, other than the reduced genome of E. coli, which would have the recited property of greatly reduced size, while remaining viable. Therefore, the specification does not describe the claimed bacteria

having reduced genome size in such full, clear, concise and exact terms so as to indicate that applicant has possession of the claimed products at the time of filing the present application. Thus, the written description requirement has not been satisfied.

Vas-Cath V. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of any bacteria having genomes that are 5, 8 or 14% smaller than the genome of the native parent strain, or which have deletions of particular genes listed in claim 5, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation or identification. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Col. Ltd.,* 18USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the E. coli strain actually disclosed in the specification, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claims 1-3 and 5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for E. coli having the recited amount of reduction of the genome size as compared to the parent strain before the reduction, does not reasonably provide enablement for any bacteria having the recited amount of genome reductions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Nature of the invention: The nature of the invention is bacteria having greatly reduced genome size when compared to the parent strain before said reduction in

genome size. Depending on the genome size, the deletions may comprise hundreds of thousands of base pairs. For instance, for E. coli with an average genome size, the greatest recited deletion consists of approximately 650,000 (650 kb) base pairs.

State of the prior art: The prior art taught the sequence of several bacterial genomes, but complete understanding of the role of all proposed open reading frames, even in the most well studied bacteria, i.e. E. coli, was not known (see page 6, Smalley et al, Trends in Microbiology, 11, (1), 6-8, 2003).

Level of predictability in the art: In order to make the bacterial strains as set forth in the instant claims, large deletions of the genome, which are not necessary for viability, must be made, and therefore, a near complete understanding of the function of large regions of the bacteria are necessary in order to obtain viable deletions of the genome. As disclosed by Smalley et al. (cited above), even in the most well studied and predictable bacteria, i.e. E. coli, it could not be predicted that any two large deletions could be combined successfully, since some mutations are "mutually exclusive" (see pages 6-7). Furthermore, the reference discloses that functional analysis of the E. coli would required coordination among many research groups, to seek a more complete understanding of particular regions of the genome. Therefore, there is much unpredictability in the art, even in bacteria whose complete sequence has been determined.

Existence of working examples: The specification provides a working example of E. coli having a reduced genome size.

Breadth of claims: The claims are broad, encompassing any bacteria having a reduced genome size (i.e. large unspecified deletions) when compared to the parent, non-deleted strain.

Amount of direction or guidance by the inventor: The specification provides little or no guidance for the methods of making large deletions in bacteria other than E. coli. The techniques used in E. coli are not clearly applicable to the other bacteria encompassed by the claims.

Quantity of experimentation needed to make or use the invention: It would require large amounts of experimentation to make the invention, since a complete or near complete knowledge of the genome's sequence would be necessary, in addition to a near complete knowledge of the structure and function of a large number of genes in the genome. Furthermore, complete knowledge of techniques genetic tools for making large, unmarked deletions would be necessary.

In summary, it would require undue experimentation to make and/or use the invention commensurate in scope with these claims. The claims should be limited to E. coli having reduced genomes when compared to the native, non deleted parent strain.

Conclusion

Claims 4, 6 and 7 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy T. Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 7:00 - 3:30, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

N. T. Vogel

Nancy T. Vogel, Ph.D.
Patent Examiner